WHAT IS CLAIMED IS:

1. An HBV variant exhibiting a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

2. The HBV variant of claim 1, carrying a mutation in the nucleoside sequence encoding a DNA polymerase resulting in an amino acid addition, substitution and/or deletion in said DNA polymerase in one or more amino acids as set forth in Formula I and/or II:

FORMULA I

L, B_1, B_2, D, W, G, P, C, B_3, B_4, H, G, B_5, H, B_6, I, R, B_7, P, R, T, P, B_8, R, V, B_9, G, G, V, F, L, V, D, K, N, P, H, N, T, B_{10}, E, S, B_{11}, L, B_{12}, V, D, F, S, Q, F, S, R, G, B_{13}, B_{14}, B_{15}, V, S, W, P, K, F, A, V, P, N, L, B_{16}, S, L, T, N, L, L, S*

wherein:

B_1 is L, or R, or I

B_2 is E, or D

B_3 is T, or D, or A, or N, or Y

B_4 is E, or D

B_5 is E, or K, or Q

B_6 is H, or R, or N,

B_7 is I, or T

B_8 is A, or S

B_9 is T or R

B_{10} is A, or T, or S

B_{11} is R, or T

B_{12} is V, or G

B_{13} is S, or I, or T, or N, or V

B_{14} is T, or S, or H, or Y

B_{15} is R, or H, or K, or Q

B_{16} is Q, or P;

and

FORMULA II

S Z_1 L S W L S L D V S A A F Y H Z_2 P L H P A A M P H L L Z_3 G S S G L Z_4 R Y V A R L S S Z_5 S Z_6 Z_7 X N Z_8 Q Z_9 Z_{10} X X X Z_{11} L H Z_{12} Z_{13} C S R Z_{14} L Y V S L Z_{15} L L Y Z_{16} T Z_{17} G Z_{18} K L H L Z_{19} Z_{20} H P I Z_{21} L G F R K Z_{22} P M G Z_{23} G L S P F L L A Q F T S A I Z_{24} Z_{25} Z_{26} Z_{27} Z_{28} R A F Z_{29} H C Z_{30} Z_{31} F Z_{32} Y M^* D D Z_{33} V L G A Z_{34} Z_{35} Z_{36} Z_{37} H Z_{38} E Z_{39} L Z_{40} Z_{41} Z_{42} Z_{43} Z_{44} Z_{45} Z_{46} L L Z_{47} Z_{48} G I H L N P Z_{49} K T K R W G Y S L N F M G Y Z_{50} I G

wherein:

X is any amino acid;

Z_1 is N or D;

Z_2 is I or P;

Z_3 is I or V;

Z_4 is S or D;

Z_5 is T or N;

Z_6 is R or N;

Z_7 is N or I;

Z_8 is N or Y or H;

Z_9 is H or Y;

Z_{10} is G or R;

Z_{11} is D or N;

Z_{12} is D or N;

Z_{13} is S or Y;

Z_{14} is N or Q;

Z_{15} is L or M;

Z_{16} is K or Q;

Z_{17} is Y or F;

Z_{18} is R or W;

Z_{19} is Y or L;

Z_{20} is S or A;

Z_{21} is I or V;

Z_{22} is I or L;

Z_{23} is V or G;

Z_{24} is C or L;

Z_{25} is A or S;

Z_{26} is V or M;

Z_{27} is V or T;

Z_{28} is R or C;

Z_{29} is F or P;

Z_{30} is L or V;

Z_{31} is A or V;

Z_{32} is S or A;

Z_{33} is V or L or M;

Z_{34} is K or R;

Z_{35} is S or T;

Z_{36} is V or G;

Z_{37} is Q or E;

Z_{38} is L or S or R;

Z_{39} is S or F;

Z_{40} is F or Y;

Z_{41} is T or A;

Z_{42} is A or S;

Z_{43} is V or I;

Z_{44} is T or C;

Z_{45} is N or S;

Z_{46} is F or V;

Z_{47} is S or D;

Z_{48} is L or V;

Z_{49} is N or Q;

Z_{50} is V or I; and

M^* is amino acid 550

and wherein S* in Formula I is designated as amino acid 420 and the first S in Formula II is designated as amino acid 421;

and wherein said variants exhibits a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

3. The HBV variant of claim 2, comprising a mutation in the nucleotide sequence encoding the HBV surface antigen which results in an amino acid addition, substitution and/or deletion in said surface antigen in a region corresponding to the amino acid sequences set forth in Formula I wherein said variants exhibits a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

4. The HBV variant of claim 3, comprising a mutation in the nucleotide sequences encoding a DNA polymerase and a mutation in the nucleotide sequences encoding the surface antigen wherein each mutation results in an amino acid addition, substitution and/or deletion to each of the DNA polymerase and surface antigen and wherein said variants exhibits a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

5. An HBV variant comprising a mutation in the nucleotide sequence encoding the HBV surface antigen which results in an amino acid addition, substitution and/or deletion in said surface antigen in a region corresponding to the amino acid sequences set forth in Formula I wherein said variant exhibits a replication fitness in the presence of a

nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

6. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analogue, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding the DNA polymerase and optionally the surface antigen (listed below in parenthesis) wherein the presence of a T474N (P120T), M550V (I195M), M550I (W196S), L526M, W499S/W499Q (G145R) mutation, or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

7. A method for detecting an HBV agent which exhibits inhibitory activity to an HBV, said method comprising:

generating a genetic construct comprising a replication competent-effective amount of the genome from said HBV contained in a plasmid vector and then transfecting said cells with said construct;

contacting said cells, before, during and/or after transfection, with the agent to be tested;

culturing said cells for a time and under conditions sufficient for the HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the virus has

replicated, expressed genetic material and/or assembled and/or been released in the presence of said agent.

8. A method for detecting an HBV agent which exhibits inhibitory activity to an HBV, said method comprising:

generating a genetic construct comprising a replication competent-effective amount of the genome from said HBV contained in or fused to an amount of a baculovirus genome effective to infect cells and then infecting said cells with said construct;

contacting said cells, before, during and/or after infection, with the agent to be tested;

culturing said cells for a time and under conditions sufficient for the HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the virus has replicated, expressed genetic material and/or assembled and/or been released in the presence of said agent.

9. A method for detecting an HBV agent which exhibits inhibitory activity to an HBV, said method comprising:

generating a continuous cell line comprising an infectious copy of the genome of said HBV in a replication competent effective amount such that said infectious HBV genome is stably integrated into said continuous cell line such as but not limited to 2.2.15 or AD;

contacting said cells with the agent to be tested;

culturing said cells for a time and under conditions sufficient for the HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the virus has replicated, expressed genetic material and/or assembled and/or been released in the presence of said agent.

10. A method of treating a patient infected with HBV, said method comprising administering to said patient an effective amount of a nucleoside analogue sufficient initially to inhibit HBV replication, monitoring HBV levels to ascertain the presence of an increased viral load in the presence of said nucleoside analogue and then changing the therapeutic protocol to permit inhibition of HBV levels.

11. A method of treating a subject infected with HBV, said method comprising administering to said subject an effective amount of FAM and/or LAM or its chemical derivatives or homologues or a functionally related nucleoside analogue for a time and under conditions sufficient for the development of HBV variants resistant to and exhibiting nucleoside analogue mediated replication fitness to said nucleoside analogue and optionally resistance to HBIG or its equivalent and then altering the therapeutic protocol to enable the inhibition of replication of the HBV variants.

12. A method of treating a subject infected in with HBV, said method comprising administering to said subject an anti-HBV agent or combination of agents which after prolonged exposure to said HBV does not select for nucleoside analogue mediated replication fitness HBV variants.

13. Use of an HBV variant which has a level of replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue in the detection of an anti-viral agent capable of inhibiting the replication of said HBV variant.

14. A computer program product for assessing the likely usefulness of a viral variant or biological sample comprising same for determining an appropriate therapeutic protocol in a subject, said product comprising:

(1) code that receives as input index values for at least two features associated with said viral agents or biological sample comprising same, wherein said features are selected from:

(a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;

(b) an altered DNA polymerase from wild-type HBV;

(c) an altered surface antigen from wild-type HBV; or

(d) morbidity or recovery potential of a patient;

(2) code that adds said index values to provide a sum corresponding to a potency value for said viral variants or biological samples; and

(3) a computer readable medium on which said codes are encoded.

15. The computer program product of claim 14, wherein the computer program product comprises a working memory, a random access memory, or a mass storage memory.

16. The computer program product of claim 14, wherein the computer readable medium comprises a magnetic medium or an optical medium.

17. The computer program product of claim 14, wherein the computer readable medium comprises a disk or a device.

18. A computer for assessing the likely usefulness of a viral variant or biological sample comprising same in a subject, wherein said computer comprises:

(1) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise index values for at least two features associated with said viral variant or biological sample, wherein said features are selected from:

(a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;

(b) an altered DNA polymerase from wild-type HBV;

(c) an altered surface antigen from wild-type HBV; or

(d) morbidity or recovery potential of a patient;

(2) a working memory for storing instructions for processing said machine-readable data;

(3) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for executing said instructions to process said machine readable data to provide a sum of said index values corresponding to a potency value for said compound(s); and

(4) an output hardware coupled to said central processing unit, for receiving said potency value.

19. The computer of claim 18, wherein the machine-readable data storage medium comprises a portion of the working memory or a mass storage memory.

20. The computer of claim 18, wherein the working memory or the machine-readable data storage medium comprises a magnetic medium or an optical medium.

21. The computer product of claim 18, wherein the working memory or the machine-readable data storage medium comprises a disk or a device.

22. A computer readable program storage medium encoded with instructions that, when executed by a computer, perform a method for assessing the likely usefulness of a viral variant or biological sample comprising same for determining an appropriate therapeutic protocol in a subject, said method comprising:

(1) obtaining index values for at least two features associated with said viral agents or biological sample comprising same, wherein said features are selected from:

(a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;

(b) an altered DNA polymerase from wild-type HBV;

(c) an altered surface antigen from wild-type HBV; or

(d) morbidity or recovery potential of a patient; and

(2) processing said index values to provide a potency value for said viral variants or biological samples.

23. The computer readable program storage medium of claim 22, wherein the computer program product comprises a working memory, a random access memory, or a mass storage memory.

24. The computer readable program storage medium of claim 22, wherein the computer readable medium comprises a magnetic medium or an optical medium.

25. The computer readable program storage medium of claim 22, wherein the computer readable medium comprises a disk or a device.

26. The computer readable program storage medium of claim 22, wherein processing said index values in the encoded method comprises adding the index values to provide a sum corresponding to the potency value.

27. The computer readable program storage medium of claim 22, wherein obtaining the index values in the encoded method comprises reading the index values from a storage or receiving the index values.

28. A computer programmed to perform a method for assessing the likely usefulness of a viral variant or biological sample comprising same for determining an appropriate therapeutic protocol in a subject, said method comprising:

(1) obtaining index values for at least two features associated with said viral agents or biological sample comprising same, wherein said features are selected from:

(a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;

(b) an altered DNA polymerase from wild-type HBV;

(c) an altered surface antigen from wild-type HBV; or

(d) morbidity or recovery potential of a patient; and

(2) processing said index values to provide a potency value for said viral variants or biological samples.

29. The programmed computer of claim 28, wherein processing said index values in the programmed method comprises adding the index values to provide a sum corresponding to the potency value.

30. The programmed computer of claim 28, wherein obtaining the index values in the programmed method comprises reading the index values from a storage or receiving the index values.

31. The programmed computer of claim 28, wherein the programmed computer comprises a desktop personal computer, a workstation, a laptop computer, a desktop computer, a mini-computer, a mainframe computer, a supercomputer, or an embedded processor.

32. A computing system programmed to perform a method for assessing the likely usefulness of a viral variant or biological sample comprising same for determining an appropriate therapeutic protocol in a subject, said method comprising:

(1) obtaining index values for at least two features associated with said viral agents or biological sample comprising same, wherein said features are selected from:

(a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;

(b) an altered DNA polymerase from wild-type HBV;

(c) an altered surface antigen from wild-type HBV; or

(d) morbidity or recovery potential of a patient; and

(2) processing said index values to provide a potency value for said viral variants or biological samples.

33. The computing system of claim 32, wherein processing said index values in the programmed method comprises adding the index values to provide a sum corresponding to the potency value.

34. The computing system of claim 32, wherein obtaining the index values in the programmed method comprises reading the index values from a storage or receiving the index values.

35. The computing system of claim 32, wherein the computing system comprises a local area network, a wide area network, a system area network, an intranet, or a portion of the Internet.